REMARKS

Claims 1-20, 37-42, and 52-53 are currently pending in the application, of which claims 12 and 13, have been withdrawn from consideration. Claims 21-36 and 43-51 have been cancelled in a previous amendment without prejudice or disclaimer to Applicants' right to pursue the subject matter of the cancelled claims in this or a subsequent application. Claims 1, 4, 14, 17, 19, and 41 have been amended to correct typographical errors. Support for the amendments to the claims can be found in the specification. No new matter has been added by the amendments to the claims.

Claims 1-11, 14-20, 37-42, 52, and 53 remain rejected under 35 U.S.C. §103(a) as being unpatentable over Bru-Magniez et al. (US 6,211,273). It is asserted that the 37 C.F.R. §132 declaration (the "Declaration") submitted by Applicants on May 31, 2005 does not provide for microparticles meeting the instant claim 1 definition, and that no correlation exists between retention of a polymer and release of drug.

Applicants disagree and respectfully traverse.

The reasoning presented in the Action fails to recognize the breadth of the instant invention. Claims 1 and 37 of the instant invention provide for a microparticle having a mean particle size of between about 1.0 μm and 100 μm. Microparticles of this size provide unique and unexpected results, such as retention in the bladder to affect controlled release of a drug. Such results are demonstrated in the Declaration and in the examples of the invention.

The Bru-Magniez patent does not teach or suggest the use of any nanoparticle for the treatment of a urological disease or disorder. Moreover, Bru-Magniez does not teach or suggest any method of treatment comprising delivery of a particulate material to the bladder or more particularly, methods of treating urological diseases or disorders (including cancer) in which microparticles having a mean particle size of between 1.0 and 100μm are administered to the lumen of a patient's bladder.

The aforementioned Declaration provides experimental data regarding microparticles of 5 μm (microspheres) and microparticles of 0.6 μm (nanospheres), and provides a comparison of microparticle retention in the bladder lumen according to microparticle size. The nanospheres are outside the scope of the instant invention and are included for reference purposes. The microspheres are encompassed by the instant invention. Experiment 4.2 provides both microparticles, experiment 4.3 discusses the procedure performed on the mice, and experiments 4.4 and 4.5 disclose the results.

Experiments 4.4 and 4.5 clearly indicate that the nanospheres are expelled from the bladder after 30 minutes. However, the microspheres are significantly retained in the bladder for up to 48 hours. Therefore, the instant invention provides the unique and unexpected result of microparticle retention in the bladder for microparticles larger than 0.6 μm.

Additionally, experiments 5.1 and 5.2 describe the use of 2 μm diameter microparticles, wherein the results are very similar to the results discovered for the 5 μm microparticles. In short, both the 2 μm microparticles and the 5 μm microparticles are significantly retained in the bladder for over 48 hours.

Regarding the allegation that no correlation exists between the retention of a microparticle and release of a drug, Applicants invite the attention of the Examiner to Example 7 of the instant application. Example 7 provides a 2 μm microparticle for antitumor activity evaluation. The results of Example 7 compare the effects of free paclitaxel against paclitaxel encapsulated in a 2 μm microparticle. The results found in Table 1 demonstrate that carcinoma in situ (CIS) is observed in 5 of 7 mice when free paclitaxel is administered. In contrast, CIS is found in 0 of 7 mice when microparticles containing paclitaxel are administered. These results suggest that free paclitaxel is quickly eliminated in urine, but a continual dosage of paclitaxel is effective in minimizing CIS. Thus, CIS is treated by the controlled release of paclitaxel in the bladder, which occurs because the microparticle is retained.

Experiments 5.1 and 5.2 of the Declaration clearly demonstrate that 2 μm diameter microparticles are retained in the bladder for up to 48 hours. Example 7 of the application as

filed shows that the antitumor drug is slowly released into the bladder, as indicated by the lack of CIS when compared to the direct administration of the free antitumor drug. Therefore, the Applicants indicate that microparticles of the instant application provide for the unexpected result of the controlled release of a drug. Further, the claims of the instant invention are not taught or suggested by Bru-Magniez for the reasons provided *supra*. For the reasons stated above, Applicants submit that the rejection should be withdrawn.

In view of the above remarks, Applicants believe the pending application is in condition for allowance. Should any of the claims not be found to be allowable, the Examiner is requested to telephone Applicants' undersigned representative at the number below. Applicants thank the Examiner in advance for this courtesy.

The Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 71699-55322.

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Respectfully submitted,

By _____

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